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Mid-term and short-term efficacy of percutaneous pharmacomechanical thrombectomy in deep venous thrombosis

Deep venous thrombosis

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Abstract
Aim: In this study, we aimed to evaluate the success and clinical results of the Mantis XP pharmacomechanical thrombectomy catheter in 64 patients.
We evaluated the efficacy and results of pharmacomechanical thrombectomy treatment in acute and subacute deep vein thrombosis.
Material and Methods: Sixty-four patients with acute or subacute deep vein thrombosis of lower extremities underwent a single-session pharmacomechanical thrombectomy between 2015 and 2018. Leg circumferences and clinical outcomes were assessed 2 years after the procedure.
Results: Body mass index was 25-30 mg/kg2 in 51.6%, 30-40 mg/kg2 in 21.9% and >40 mg/kg2 in 2% of the patients.When leg circumferences were evaluated during and 2 years after the procedure, a significant reduction in circumference was found both at thigh and calf level (p<0.001).
Discussion: Pharmacomechanical thrombolytic treatment is based on interventional lysis of endovenous thrombosis and emerged as an alternative to open surgery, thrombectomy, and catheter-directed thrombolysis. Pharmacomechanical thrombectomy is safe and effective in the treatment of deep vein thrombosis.

Keywords
Venous thromboembolism; Thrombectomy; Thrombolysis; Mechanical thrombectomy

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Introduction

Venous thromboembolism has an annual incidence rate as high as 1-2 per 1000 and usually appears in the form of deep vein thrombosis (DVT). Approximately 20% of patients with symptomatic DVT develop "post-thrombotic syndrome (PTS)" with chronic leg pain, swelling, venous stasis, and leg ulcers [1]. PTS is the main underlying reason of the high morbidity, poor quality of life, and socio-economic losses in the long term. The conventional treatments used for the prevention of PTS in patients with DVT are not yet considered sufficiently successful enough.

It has been demonstrated that DVT patients with iliofemoral segment involvement, in particular, have higher rates of PTS and lower quality of life when they are treated with anticoagulants alone [2].

The anticoagulants used in the standard treatment are known to reduce pulmonary embolism and mortality, while they were shown not to decrease the PTS risk since they do not reduce existing thrombus burden [3].

Some studies reported a PTS rate of 20-50% and a venous ulcer rate of 5-10% following standard anticoagulant treatment [4].

Systemic thrombolytic agents have found no place in the treatment of DVT due to their side effects such as bleeding.

Recently, catheter-mediated thrombolysis and pharmacomechanical thrombectomy devices have been used to reduce the high PTS rates. Thereby, the high bleeding risk associated with the use of thrombolytic agents is avoided by administering lower doses of these agents directly into the thrombus. It was shown that the reduction of thrombus burden with the use of catheter-mediated thrombolysis and other FMT devices can be effective in the prevention of permanent venous obstruction and venous valve damage [4,5]. Early reduction in thrombus load with this method is a promising strategy to decrease venous hypertension and the rate of PTS with the prevention of venous valvular damage.

Recently, endovenous catheter-mediated pharmacomechanical thrombolysis (PMT) procedures are being performed in an increasing number of centers and particularly as the first choice in the treatment of iliofemoral DVT in some clinics. Growing experience and favorable results with PMT have made it a more widely used method in the light of the high rate of PTS.

While the short-term results of PMT are favorable, there are limited studies on the long-term results.

In this study, we aimed to present the mid- to long-term results in terms of PTS in patients undergoing PMT. Moreover, the association between mid- to long-term results and various parameters, including etiology, gender, and body mass index were evaluated in this study.

Material and Methods

Sixty-four patients (32 males and 32 females) presenting with only acute or subacute iliofemoral DVT who were treated with PMT (Mantisxp Thrombectomy Device, İnvamed, TR) between 2015 and 2018 were included in the study.

All patients presented to the emergency service or outpatient clinic with complaints of leg pain and swelling and were hospitalized with the definitive diagnosis of DVT made using Doppler ultrasonography. All patients had high (femoral and/or iliac vein) deep vein thrombosis. The mean age of the patients was 49.5 years (range 17-77 years).

Patients with recurrent DVT, DVT at a lower level, symptom duration of more than 2 weeks, life expectancy of less than 1 year, and/or additional risk factors for thrombolytic therapy were excluded.

PMT Procedure:

Patients considered for PMT underwent the procedure under local anesthesia at the interventional radiology unit after providing informed consent. The vena cava filter was placed below the renal vein via the femoral vein with the patients in the supine position and then the patients were turned into the prone position (Figure 1). A 0.35-inch guidewire was inserted into the involved popliteal vein with percutaneous puncture under US guidance while the patients were in the prone position, and then a 7-Fr sheath was inserted into the popliteal vein via the guidewire. The occluded venous segments were assessed with venography performed through the sheath in the popliteal vein. The PMT thrombectomy procedure was then performed with tPA infusion by inserting a 6-F thrombectomy catheter (Mantisxp Thrombectomy devices) through the sheath in the popliteal vein and gradually advancing the catheter first to the inguinal level and then into the iliac veins (Figure 2). Optimal patency was tried to be achieved by applying the same procedure to the regions with inadequate patency on venograms performed after thrombectomy. The procedure was terminated in patients with adequate patency and these patients were followed up in the ward for potential complications.

In patients hospitalized for PMT, LMWH treatment (bemiparin sodium, 115 IU/kg, SC, once daily) was initiated immediately after the diagnosis and PMT was performed as soon as possible. In patients with no post-PMT complications, oral warfarin was initiated on top of LMWH treatment with regular INR measurements and LMWH treatment was stopped and oral warfarin treatment was continued when INR was >2. Patients who achieved effective INR levels were discharged on oral warfarin with advice to use compression stockings. Patients were followed up at 3-month intervals and remained on warfarin treatment for at least 6 months after discharge. Patients were advised to use compression stockings for 2 years. Calf and thigh circumferences of the patients were measured and patients were asked to assess their pain levels on the pain scale before and 24 hours after the procedure and every 6 months thereafter. Control Doppler US examination was performed at 6-month intervals.

Statistical Analysis:

Statistical analyses were performed using IBM software SPSS 22 (IBM Corp., Armonk, NY, USA). The variables were evaluated using visual (histograms, probability plots) and analytic methods (Kolmogorov-Smirnov /Shapiro-Wilk test) to determine whether or not they are normally distributed. Descriptive analyses were presented using means and standard deviations for normally distributed variables. Frequencies and percentages were given for categorical and nominal variables. Repeated measures analysis of variance was used to explore the effect of the procedure (PMT) on the change in thigh and leg circumferences. The Chi-square test or Fisher's exact test, where appropriate, was used to compare the proportions of Doppler US findings

and pain scale categories and also to compare gender and thrombus status during follow-up. A p-value of less than 0.05 was considered to show a statistically significant result.

Results

The mean follow-up was 24.38 months (range 3-40 months). All patients had thrombosis at the iliofemoral level with a symptom duration of less than 2 weeks. Twenty-eight patients (43.8%) had right and 36 patients (56.3%) had left lower extremity involvement. DVT etiologies are presented in Table 1.

Thirty-one patients (48.4%) had history of smoking. Body mass index was 25-30 mg/kg2 in 51.6%, 30-40 mg/kg2 in 21.9% and >40 mg/kg2 in 2% of the patients.

After the PMT procedure, 5 patients developed hematoma in the popliteal region and only one of these patients required surgical exploration and vascular repair. In the remaining 4 patients, hematoma regressed with compression. One patient developed complaints similar to contrast allergy but these complaints were resolved in a short time without requiring any medication. None of the patients had severe bleeding. Almost all patients experienced a dramatically marked decrease in pre- and postprocedural pain. Pain scores measured before, after, and at 2 years after the procedure are presented in Figure 1. Significant differences were found between preprocedural, postprocedural, and 2-year measurements ($p<0.001$) (Figure 3a).

When preprocedural, post-procedural, and 2-year leg circumferences were evaluated, significant reductions in circumference were found both at thigh- and calf-levels ($p<0.001$) (Figure 3b). Control US examinations of the patients revealed that the patients with scores of 3-4 on the pain scale at 2 years had US findings consistent with thrombus and this relationship was statistically significant ($p<0.001$). Two of these patients developed stasis dermatitis during follow-up.

No significant relation was found between control US findings and the etiological classification of DVT ($p>0.05$). Gender and age were not significantly related to control US findings and pain.

Table 1. DVT etiology

Etiological reasons	n	%
Unknown	17	26.6
Immobilization	6	9.4
Previous Surgery	20	31.3
Genetic	6	9.4
Other	15	23.4
Total	64	100

Discussion

Early diagnosis and treatment of DVT complications are critical since they lead to high mortality and morbidity rates and long-term work loss and require long-term and expensive treatments. PMT should be used in patients with an active life, phlegmasia cerulea dolens, early diagnosis (acute or subacute), and iliofemoral involvement.

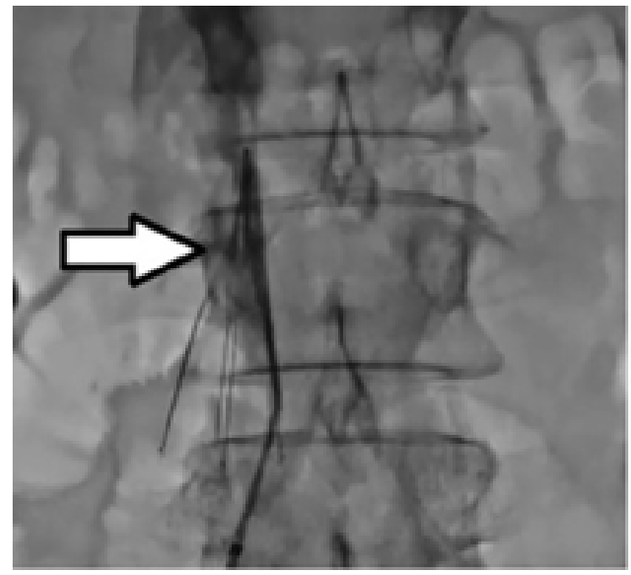

Figure 1. Implantation of IVC filter

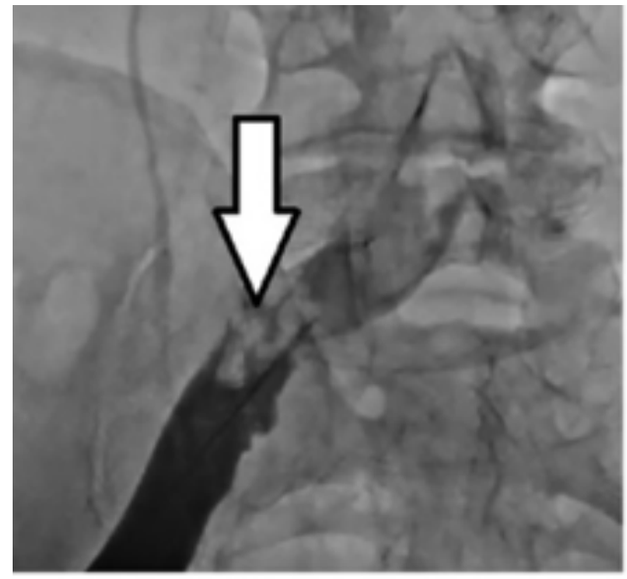

Figure 2. Lysis of the thrombus in the iliac vein with PMT catheter

The short-term results of PMT, which is increasingly more commonly used in patients with high DVT, are pleasing, while its long-term results, particularly with respect to PTS, are still unclear. Many studies reported an unacceptable long-term PTS rate of 25-46% with classical anticoagulant treatment alone in iliofemoral DVT. There are studies showing that the PTS risk during 5-year follow-up periods is reduced by the use of PMT [6,7].

DVT is caused by immobilization, surgery, trauma, older age, malignity, factor deficiencies (protein c-protein s-antithrombin), factor V mutation and medications such as oral contraceptives. The American Venous Forum's suggestion that 'PMT should be performed within 14 days of symptom onset' may explain the favorable results in terms of both PTS and venous patency [8,9]. Conventional treatment involves the use of warfarin, low-molecular-weight heparin or NOACs. Recently, PMT, thrombolysis, and similar methods have started to be used.

In our study, control US examinations and pain and leg circumference evaluations performed during mid- to long-term

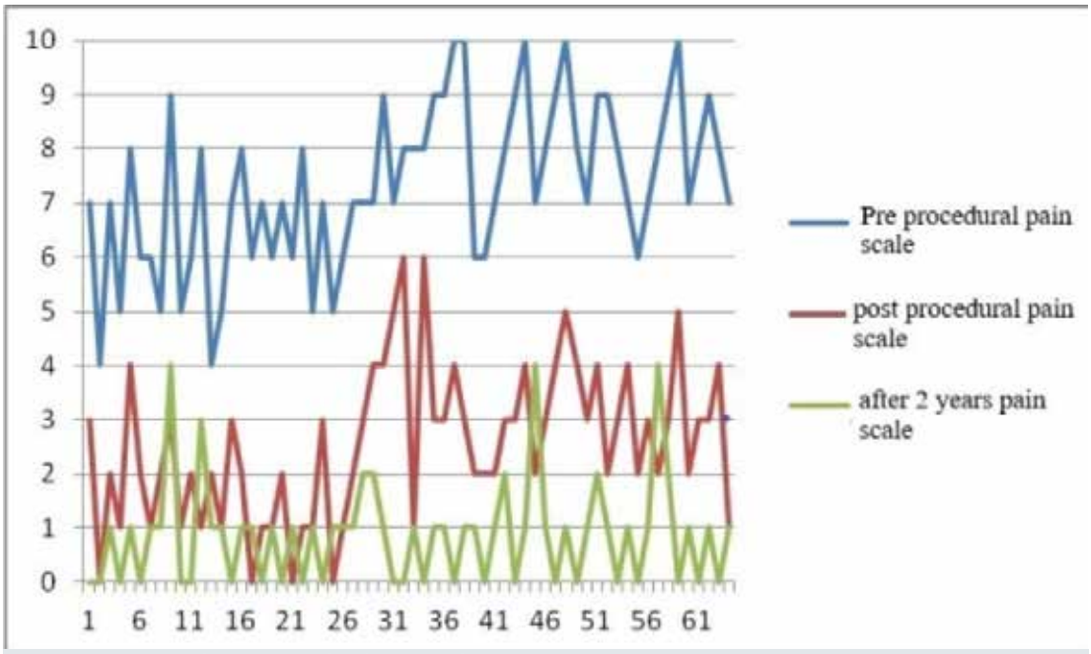

Figure 3a. Pre- and post procedural pain scale

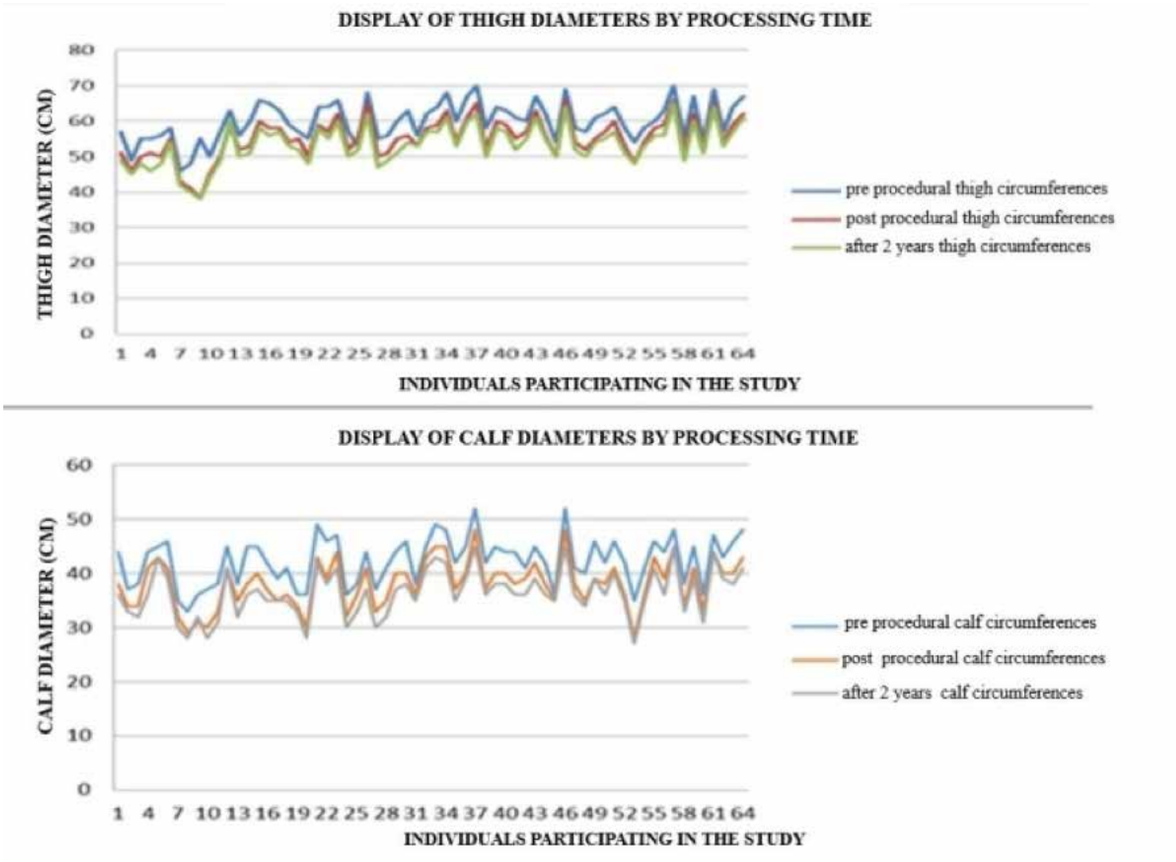

Figure 3b. Changes in thigh and calf circumferences after two years

follow-ups after the PMT procedure revealed a rate of 10.9% for PTS findings. Two patients had stasis dermatitis. This suggests that this rate may increase even further with longer follow-up.

Pharmacomechanical thrombolytic treatment (PMT) is based on the interventional lysis of endovenous thrombosis and emerged as an alternative to open surgery, thrombectomy, and catheter-directed thrombolysis (CDT). Although the long-term effects of this treatment have not been reported in the multicenter randomized controlled studies published so far, observational studies have reported successful PMT practices [10].

There is consensus on the use of CTD or thrombolytic treatment in addition to PMT treatment in patients without contraindications [11-12].

Recent studies reported that IVC (inferior vena cava) filter reduces the risk of pulmonary embolism [13, 14]. In our study, all patients were successfully implanted with an IVC filter. Filters were removed from all except two patients. We believe that

the IVC filter should be routinely used in all patients, despite the manual aspiration feature of the Mantis PMT catheter. The catheter aspirates blood clots near its lumen, but this is not sufficient in segments with higher thrombus loads, since it moves centripetally in the direction of the flow.

When PTS is evaluated in relation to the open vein hypothesis, venous patency was found in 92.1% of our patients. We believe that this resulted from the admission of the patients in acute-subacute phase and from the thrombus quality.

In general, symptom duration for more than 10 days was reported to reduce the rate of complete thrombus resolution [15,16].

Another conclusion of this study is that this procedure provides quite satisfactory thrombus resolution as well as significant symptomatic improvement.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

References

1. Ho WK, Hankey GJ, Lee CH, Eikelboom JW. Venous thromboembolism:diagnosis and management of deep venous thrombosis. Med J Aust 2005;182(9):476-81.

2. Kahn S, Shrier I, Julian J, Ducruet T, Arsenault L, Miron M-J, et al. Determinants and time course of the postthrombotic syndrome after acute deep venous thrombosis. Ann Intern Med. 2008;149(10):698-07.

3. Sharafuddin MJ, Sun S, Hoballah JJ, Youness FM, Sharp WJ, Roh BS, et al. Endovascular management of venous thrombotic and occlusive diseases of thelower extremities. J Vasc Interv Radiol. 2003;14:405-23.

4. Schulman S, Lindmarker P, Holmstrom M, Lärfars G, Carlsson A, Nicol P, et al. Post-thrombotic syndrome,recurrence, and death 10 years after the fi rst episode of venous thromboembolism treated with warfarin for 6 weeks or 6 months. J Thromb Haemost. 2006; 4(4): 734–42.

5. Enden T, Wik HS, Kvam AK, Haig Y, Kløw NE, Sandset PM, et al . Health-related quality of life after catheter-directed thrombolysis for deep vein thrombosis: secondary outcomes of the randomised, non-blinded, parallel-group CaVenT study. BMJ Open. 2013;3(8):e002984.

6. Van Dongen CJJ, Prandoni P, Frulla M, Marchiori A, Prins MH, Hutten BA. Relation between quality of anticoagulant treatment and the development of the postthrombotic syndrome. J Thromb Haemost. 2005;3(5): 939-42.

7. Haig Y, Enden T, Grøtta O, Kløw N-E, Slagsvold C-E, Ghanima W, et al. Post-thrombotic syndrome after catheter-directed thrombolysis for deep vein thrombosis (CaVenT): 5-year follow-up results of an open-label, randomised controlled trial. Lancet Haematol. 2016;3(2): 64-71.

8. Meissner, MH Gloviczki P, Comerota AJ, Dalsing MC, Eklof BG, Gillespie DL, et al. Early thrombus removal strategies for acute deep venous thrombosis: Clinical Practice Guidelines of the Society for Vascular Surgery and the American Venous Forum. J Vasc Surg. 2012;55(5):1449-62.

9. Cohen AT, Agnelli G, Anderson FA, Arcelus JI, Bergqvist D, Brecht JG, et al. VTE Impact Assessment Group in Europe (VITAE). Venous thromboembolism (VTE) in Europe. The number of VTE events and associated morbidity and mortality. Thromb Haemost. 2007; 98(4):756-64.

10. Köksoy C, Yılmaz MF, Başbuğ HS, Calik ES, Erkut B, Kaygın MA, et al. Pharmacomechanical Thrombolysis of Symptomatic Acute and Subacute Deep Vein Thrombosis with a Rotational Thrombectomy Device. J Vasc Interv Radiol. 2014; 25(12): 1895–900.

11. Mewissen MW, Seabrook GR, Meissner MH, Cynamon J, Labropoulos N, Haughton SH. Catheter-directed thrombolysis for lower extremity deep venous thrombosis: report of a national multicenter registry. Radiology. 1999; 211(1): 39–49.

12. McLafferty RB. Endovascular management of deep venous thrombosis. Perspect Vasc Surg Endovasc Ther. 2008; 20(1): 87-91.

13. Sharifi M, Bay C, Skrocki L, Lawson D, Mazdeh S, et al. Role of IVC filters in endovenous therapy for deep venous thrombosis: the FILTER-PEVI (Filter Implantation to Lower Thromboembolic Risk in Percutaneous Endovenous Intervention) trial. Cardiovasc Intervent Radiol. 2012; 35(6): 1408–13.

14. Karthikesalingam A, Young EL, Hinchliffe RJ, Loftus IM, Thompson MM, Holt PJE. A Systematic Review of Percutaneous Mechanical Thrombectomy in the Treatment of Deep Venous Thrombosis. Eur J Vasc Endovasc Surg. 2011;41(4):554-65.

15. Park SI, Lee M, Lee MS, Kim MD, Won JY, Lee DY. Single-session aspiration thrombectomy of lower extremity deep vein thrombosis using large-size catheter without pharmacologic thrombolysis. Cardiovasc Intervent Radiol. 2014;37(2):412–19.

16. Rosfors S, Noren A. Venous Haemodynamics and Morphology in Relation to Recanalisation and Thrombus Resolution in Patients with Proximal Deep Venous Thrombosis. Phlebology. 1999;14:33-8.

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